

Zika Virus in Placental Villi at 28 Weeks of Pregnancy

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Summary

The aim of this study was to examine the structure of the placental villi associated with Zika virus at 28 weeks of pregnancy without another antecedent of illness and to be evaluated with light microscopy. Two groups of population of placental villi were taken of placenta study and placenta normal. The group studies proceed of placenta obtained at 37 weeks by caesarian delivery with fetal suffering. The placenta normal was obtained at 38 weeks with an increase of weight of woman pregnancy of 10 Kg both being processed according to previous works realized. The decidual region and stem villi showed infiltration of mononuclear cells. Stem villi were observed with thrombotic vessels, fibrinoid deposition, vascular obliteration, trophoblast necrosis and fibrosis. Zones of immature intermediate villi were seen suffering degenerative changes. Clear zones appeared in the stromal region of the placental villi. Mature intermediate villi have not bends and are absent of terminal villi. Numerous syncytial nodules are showed in zones of microinfarcts. Bad development of the ramifications of the placental villi is noted. These results indicate a destructive and generalized effect on the structure of the placental tree as also it has been affected by others viruses which damage the placenta contributing with fetal suffering or fetal death.

Keywords

Light microscopy; Zika virus Placental; Villi 28 weeks

Introduction

Since that the first human Zika virus (Zikv) infection was reported in Uganda in 1964 a numerous publications about epidemiological aspects, evolution of the viral activity, modes of transmission and their clinical and historic consideration have been described [1]. Zikv is an emerging arbovirus, flavivirus of the family flaviviridae which includes Dengue, West Nile, Yellow fever and Japanese encephalitis viruses that implicate an expanding threat in public health [2].

Zikv is known as a neurotropic microorganism that provokes neurological complications as encephalopathy and microcephaly [3-5]. It can be detected in plasma and urine but the mechanism of flavivirus infection is not clearly understood and pathology depends on the virus [4]. We not know if placental involvement of Zikv described in a preliminary report could be caused by direct damage to the placenta by the virus or provoked by an immune mediated response [6].

When there is intrauterine infection by Zikv fetal ultrasound examination shows brain calcifications in fetal brain parenchyma although in our observations of the placental tree they have been absent. Zikv can to be present in concurrent outbreaks of dengue; chikungunya and zika virus infections but the histopathologic changes on the human placental villi have been few described [6-9].

Only have been indicated clinical, epidemiological and historic data. Zikv is transmitted by arthropods vectors of the *Aedes* genus. *Aedes albopictus* was the first description as potential vector in 2007 [10].

Zikv directly infect the placental barrier provoking the disrupting of the syncytial plasma membrane with viral replication in citotrophoblast and Hofbauer cells which are permissive to Zikv infection [11].

If well type III interferons produced by human placental trophoblast confer protection against Zika virus infection data suggest that Zikv when access the placental villi it must evade this restriction [12].

The Hofbauer cells have been observed in proliferation within the stromal region with hyperplasia but without inflammation [13].

During the first trimester of pregnancy Zikv replicate in a wide range of maternal

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and fetal cells, including decidual fibroblast and macrophages, trophoblasts, Hofbauer cells and umbilical cord mesenchymal stem cells indicating cellular tropism and its cytopathic induced tissue injury [14].

Trophoblast of the early first trimester of pregnancy are highly susceptible to infection by Zikv however the cells isolated from term placentas are in a strong position to minimize infection and viral replication [15].

This infection is associate to low-grade fever, arthralgia, notably of small joints of hands and feet, with possible swollen joints, myalgia, headache, retroocular headaches, conjunctivitis and cutaneous maculo-papular rash [3]. Besides, abdominal pain, diarrhea, constipation, mucous membrane ulcerations and pruritus [16]. When is complicated with preeclampsia, megaloblastic macrocitic anemia and marginal insertion of umbilical cord can to contribute with the death early of the fetus [17].

The initial discoveries of the virus were identified from pregnant brazilian women whose amniotic fluid tested positive for the Zikv and were later established in the fetuses which further confirmed the possible relationship between the Zikv and the causes of microcephaly [18-20].

To compare the results obtained a week before parturition of this infection with the observed in this work at the 28 weeks of pregnancy is our proposal [6].

Material and Methods

Two groups of population of placental villi were taken of placenta study and placenta normal, the group study proceed from hospitality institution whose placenta was obtained to the 37 weeks by caesarean delivery with fetal suffering. Infection by Zikv occurred to 28 weeks with fever, arthralgia, maculo-papular eruption and adenopathies. Infection was confirmed by National Institute of Hygiene-Caracas. Serology of patient was negative for another microorganism. Without other metabolic disease, genetic, parasitary, or with bad-formation and being sero-negative to the six weeks of birth.

The infected woman pregnancy had knowledge of informed consent and approval by ethical committee of the hospitality institution for realization of this investigation according to the Helsinki declaration. The placenta normal was obtained at 38 weeks of patient with an increase of weight of 10 kg without antecedent of disease.

Of each placenta were taken five small specimens of the maternal surface selected to the azar from the region central parabasal in the vertical plane. Three slides by specimen were prepared for light microscopy and 30 histological slides in total were stained with H&E for their observation. The concepts of immaturity, edema, fibrinoid deposition are used as in previous works [6,21,22].

Results

With frequency thrombotic vessels of stem villi were observed, these villi are surrounded by a ring of fibrinoid deposition (Figure 1). Mature intermediate villi have not bends in their trajectory and they are absent of terminal villi (Figure 2).

Bad developments of the ramifications of the placental villi are noted (Figure 3). Stem villi were seen with vascular obliteration, trophoblast necrosis and fibrosis (Figure 4). Regions of infarcts were found (Figure 5).

Numerous immature intermediate villi show syncytium in degeneration (Figure 6). The decidual region and stem villi when seen showed infiltration of mononuclear cells (Figure 7).

In some villi the stromal region is exhibited with regions more clear where the lytic effect of the viral activity could provoke damage (Figure 8). Mononuclear cells also are located in the intervillous space and debris of syncytium are seen between villi with severe degenerative changes (Figure 9).

Numerous syncytial nodules are showed in the surface of the placental villi (Figure 10). Zones of immature intermediate villi were found (Figure 11).

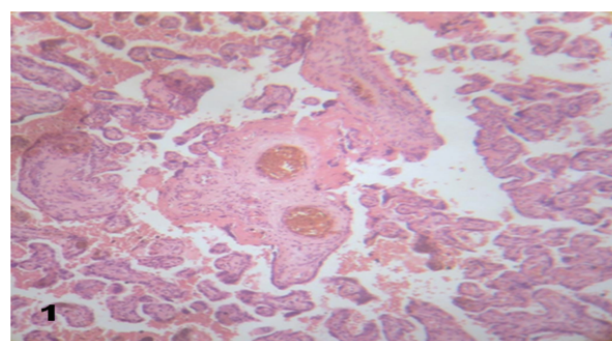


Figure 1: Thrombosis of stem villi is observed. H&E. 160x.

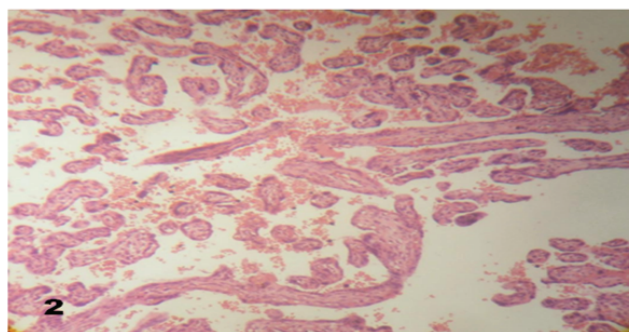


Figure 2: Mature intermediate villi are noted without terminal villi. H&E. 160x.

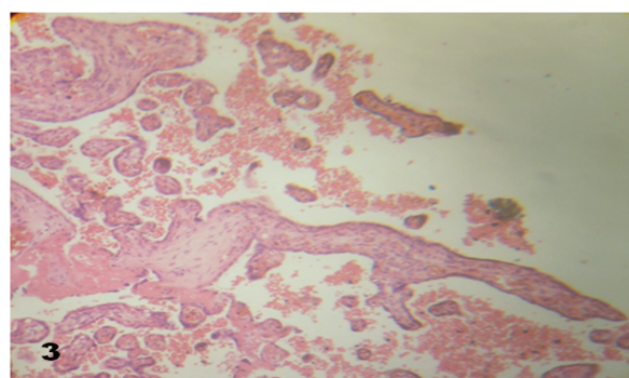


Figure 3: Ramifications of the placental villi present bad development. H&E. 160x

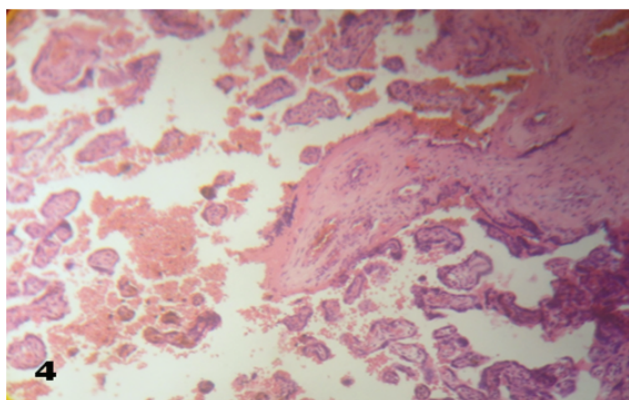


Figure 4: A fibrotic stem villi is observed. H&E. 160x

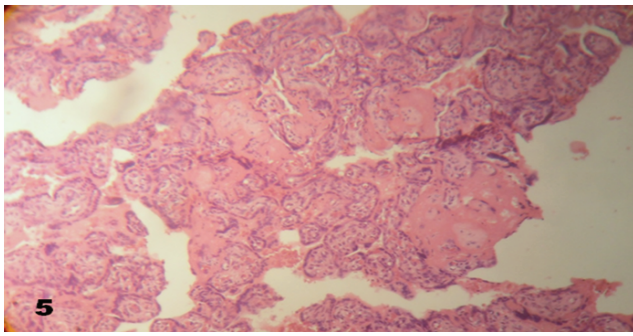


Figure 5: Regions of microinfarcts are seen. H&E. 160x.

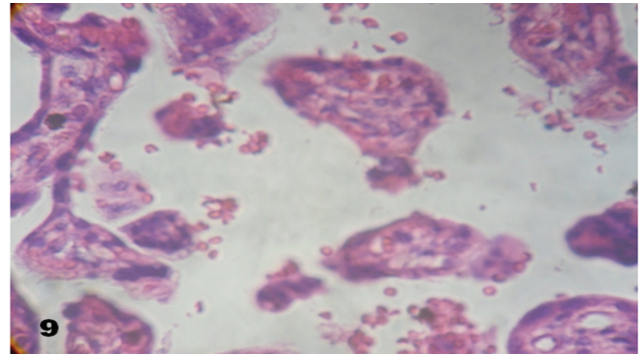


Figure 9: Several debris of syncytium are found in the intervillous space. H&E. 640x.

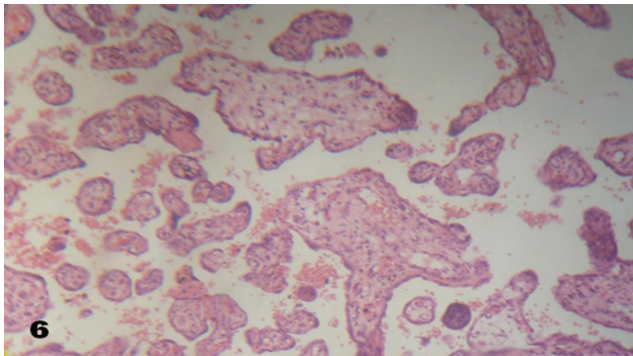


Figure 6: Immature placental villi shows syncytial degenerative changes. H&E. 160x.

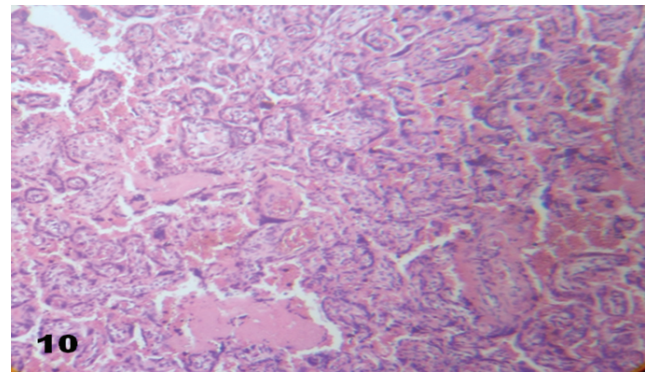


Figure 10: Syncytial nodules can be observed on the surface of the placental villi. H&E. 160x.

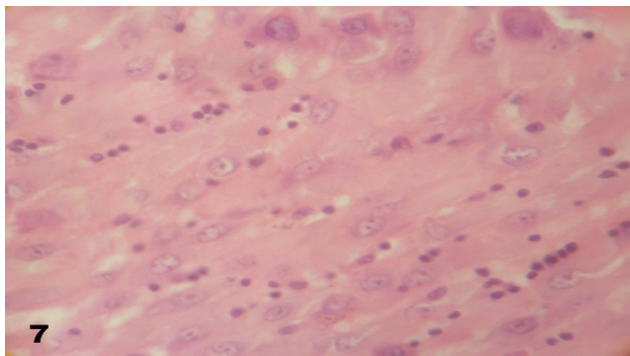


Figure 7: An infiltration of mononuclear cells is noted in decidual region. H&E. 640x.

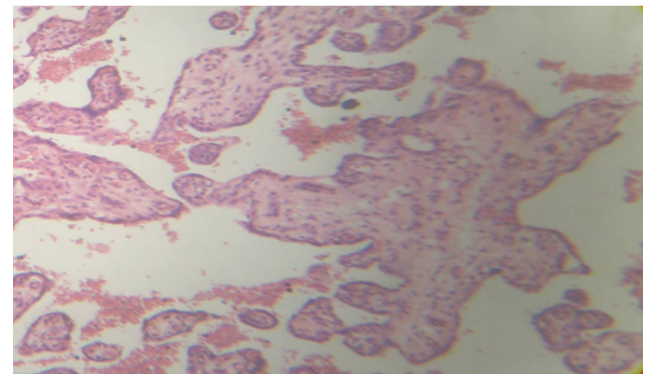


Figure 11: Zones of immaturity are noted. H&E. 160x.

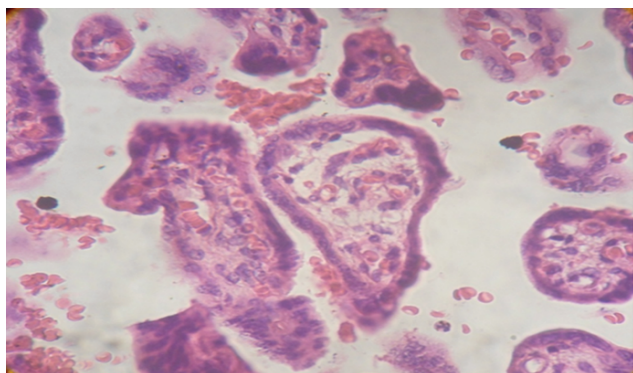


Figure 8: Regions more clear are observed in the stroma of placental villi. H&E. 640x.

Discussion

Thrombotic vessels were found in this case with Zikv infection at the 28 weeks which differs of the observed a week before parturition [6]. Probably the formation of thrombus occurs when damage to endothelial cells of the placental villi by Zikv lead to the production of cytokines and provokes an immune response, causing inflammation. This can lead to the formation of a plaque covered by a fibrous cap-if the cap breaks, the contents of the plaque is released, causing thrombosis. There are virus as herpes virus that can make atherosclerosis [23]. In the before case the placenta not had time for the formation of these events.

Mature intermediate villi maintains the same characteristics observed in the preliminary report [6]. With this absence of terminal villi could be in danger the life of the fetus since the interchange of nutrients and gases are realized in this structure [24]. Bad

development of the ramifications of the placental tree also have been observed when the placenta was associated to preeclampsia severe, megaloblastic anemia, infection by Zikv at 14 weeks of pregnancy, marginal insertion of umbilical cord and to a week before parturition [6,17].

Stem villi with vascular obliteration, trophoblast necrosis and fibrosis of placental villi have been observed in infection by cytomegalovirus accompanying severe inflammation of the villi or villitis as occurred in this case [24]. The thrombotic formation here seen has caused low blood flow which lead to the observation of numerous regions of infarcts.

Zikv infection appear to produce placental immaturity seen also in infection by Chikungunya virus; an arbovirus of the togaviridae family [22]. The deciduitis noted in decidual region is common in these viral infections which permit the rapid diffusion to the placental region as has been observed in pregnant rhesus macaques [25].

All the types of placental villi are suffering the effect of the infection by Zikv. When there is coinfection of Zikv with another virus as herpes simplex virus -2 (HSV-2) increases the risk for Zikv infection provoking a higher apoptosis in placenta of first-trimester [26]. This produce degenerative changes a level of the trophoblast as necrosis of the syncytium, interruption, thinning and syncytial nodules. Stromal region suffers severe lytic changes observing completely hyalinized zones, contributing with a destructive villitis.

This effect is associated to grave outcomes during pregnancy including fetal death, placental insufficiency, fetal growth restriction and central nervous system injury [27,28]. This viral attack not permit the development complete of the ramifications of the placenta and the placental tree stay with zones of immaturity indicative of delay of villous maturation.

This placental immaturity has also been described in cases of infection with HIV/HPV, Chikungunya virus and VIH by us [6]. Zikv infection has produced a destructive and generalized effect on the structure of the placental tree which is evident by the cellular detritus which are observed in the intervillous space between villi that are suffering severe degenerative changes. Human and institutional general intents are being realized for to avoid and to control this effect [27].

In conclusion, the infection by Zikv affect the placental tree as also it is affected by others viruses which damage the placental structure contributing with fetal suffering.

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